

REMARKS/ARGUMENTS

This is in response to the Examiner's communication mailed July 2, 2003.

Claims 126 to 134 have been withdrawn from consideration.

The Examiner rejects the pending claims under 35 USC 112, second paragraph, stating that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. In particular, the Examiner states that the specification does not teach what a weak promoter is and that a certain promoter must be specified in the claims. Applicant traverses this rejection.

The claims recite a "promoter weak relative to a T7 promoter." The specification discloses the use of a T7lac promoter to produce soluble, recombinant botulinum toxin proteins. A practitioner of ordinary skill in the art recognizes that a T7lac promoter is a weak promoter relative to a T7 promoter. In addition, reporter systems are readily available which can assess the strength of promoters. Such reporter systems are well known to practitioners of ordinary skill in the art. Thus, whether a promoter is weak relative to a T7 promoter can readily be determined by one of ordinary skill in the art from the measurements provided using these well known reporter systems. Therefore, promoters that are weak relative to a T7 promoter can easily be identified by a practitioner of ordinary skill in the field without undue experimentation.

In addition, dependent claims 118 and 120 do recite certain promoter types, i.e., an inducible promoter and a T7lac promoter respectively.

The Examiner also indicates that the claims are incomplete for omitting essential steps. The Examiner contends that culture

conditions such as inducing time and temperature and a step of purification are essential elements of the claims.

Applicant disagrees with the Examiner and submits that particular culture conditions and a purification step are not essential in the production of the soluble botulinum toxins as claimed.

Various culture conditions may be employed without significantly effecting the production of soluble, recombinant botulinum toxin proteins as described in the specification. As is understood by a practitioner of ordinary skill in the art, conditions such as time of induction and growth temperature can be varied substantially without preventing the production of the soluble, recombinant proteins produced with a particular expression system. The specification includes a growth temperature of 37°C and an induction time of 2 hours. However, this incubation temperature and induction time are not essential in the method.

A step of purification also is not an essential step in the methods. The claims state a method of producing soluble botulinum toxin and do not specify a purified or partially purified protein product.

In view of the above, applicant submits that claims 113 to 125 satisfy the requirements of 35 USC 112, second paragraph, and respectfully requests that the rejection of these claims based on this statutory provision be withdrawn.

The Examiner rejects claims 113, 114, 116 and 119 under 35 USC 112, first paragraph, stating that a skilled artisan would have to conduct undue and excessive experimentation in order to practice the claimed invention. This is an enablement rejection. The Examiner indicates that adequate guidance is not provided to select a weak promoter to produce the botulinum

toxin in soluble form. The Examiner also rejects the claims as overly broad stating that the claims encompass any prokaryotic vector with any weak promoter in any host cell. Applicant traverses these rejections.

Applicant submits that an important feature for producing a soluble, recombinant botulinum toxin is promoter strength as determined by Dr. Williams. The claims include the feature of "a weak promoter relative to a T7 promoter" for producing the soluble botulinum toxin proteins. As discussed above, it is within the skill of a practitioner of ordinary skill, or a technician, in the field to test promoters that are weak relative to a T7 promoter for soluble botulinum toxin production. In addition, the feature of "any weak promoter" is not present in the claims.

The invention is not limited to any particular host cell. For example, on page 26, lines 3 to 8 of the specification it is stated that: "The present invention is not limited by the nature of the host cell employed for the production of recombinant *C. botulinum* toxin proteins. In a preferred embodiment, the host cell is an *E. coli* cell. In another preferred embodiment, the host cell is an insect cell; particularly preferred insect host cells are *Spodoptera frugiperda* (Sf9) cells. In another preferred embodiment, the host cell is a yeast cell; particularly preferred yeast cells are *Pichia pastoris* cells."

The invention is not limited to any particular vector. Vectors that may be used in accordance with the present invention include those which encode a weak promoter relative to a T7 promoter as expressed in a prokaryotic expression system. However, a vector for use in the present invention is not selected based solely on the strength of the promoter encoded by the vector. One or more other factors known to those of

ordinary skill in the art may also be employed to select a particular vector. For example, as is known to one of ordinary skill in the art, different host cells typically require different vectors. Therefore, since the invention is not limited to a particular host cell, the invention also is not limited to a particular vector.

The selection of useful host cells and vectors is well within the ordinary skill in the art, particularly in view of the disclosure set forth in the above-identified application.

Moreover, requiring applicant to limit the invention to a certain host cell and/or a certain vector is an unjustified and improper restriction on the scope of the present claims.

In view of the above, applicant submits that claims 113 to 125 satisfy the requirements of 35 USC 112, first paragraph, and respectfully requests that the rejection of these claims based on this statutory provision be withdrawn.

Applicant submits that claims 113 to 124 comply with the first and second paragraphs of 35 U.S.C. 112 and are therefore allowable. Applicant therefore respectfully requests that the Examiner pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Respectfully submitted,



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